

REMARKS/ARGUMENTS

I. Status of the claims

Claims 15-28 are canceled. The application was not filed with claims 1-14. After a phone conversation with the Examiner on March 14, 2005, it was agreed that Applicants would cancel the present claims and add new claims beginning from claim 1. Accordingly, new claims 1-14 and 32-39 are added with this amendment. Claims 1-6 and 32-39 are currently under examination. The subject matter of claims 7-14 and 29-31 was restricted by the Examiner.

II. Support for the Amendments

Support for the claims can be found in the specification and original claims as filed. The claims are re-written versions of original claims 14-30. Accordingly, claim 1 finds support in original claim 15. Claim 3 finds support in original claim 17.

Support for claims 2 and 4 can be found on, e.g., page 6, lines 18-19 of the specification.

Claims 5-14 and claims 29-31 find support in original claims 5-30, respectively.

Support for "a second oligonucleotide carrying a FRET acceptor entity but not carrying a donor entity" as recited in claims 1-3, can be found throughout the specification and examples. The examples in particular describe two oligonucleotides, one labeled with fluorescein and nitroindole and the other carrying LC-Red-640 (an acceptor) and lacking a donor. *See, e.g.*, page 13, lines 25-28 of the specification. Moreover, the specification repeatedly refers to examples of three oligonucleotides in which the first and third oligonucleotides comprise a FRET pair consisting of a donor and an acceptor. *See, e.g.*, page 8, lines 5-15 of the specification. By indicating that the entities were a FRET pair and are on two different oligonucleotides, it is clear that there is not another donor on the oligonucleotide carrying the acceptor.

Claims 32-39 are analogous to original claims 15-20 but include the nitroindole moiety as the quencher. Support for use of nitroindole can be found, e.g., in the Examples.

No new matter is added by the amendment.

III. Status of claims 1-14

As noted above, the application was not filed with claims 1-14. After a phone conversation with the Examiner on March 14, 2005, it was agreed that Applicants would cancel the present claims and add new claims beginning from claim 1. Applicants thank the Examiner for noting this issue.

IV. Priority

The Examiner indicated that a certified copy of the European priority application had not been received. Applicants submitted a certified copy on September 2, 2004.

V. Specification

The Examiner objected to the disclosure because the application referred to Figures "1" and "2", whereas that drawings are labeled "1A", "1B", etc. Applicants have amended the specification to correct this issue. Accordingly, Applicants respectfully request withdrawal of the rejection.

VI. Claim objections

Claim 1 was objected to because "FRET" is an abbreviation. As amended, when "FRET" is first used in claim 1, the full term is written out.

Claims 16 and 18 were objected to for reciting "quenching fluorescence emission." As amended, new claims 1-2 do not recite "emission".

Accordingly, Applicants request withdrawal of the objections.

VII. Rejection under 35 USC § 112, first paragraph

Claims 16 and 18 were rejected under 35U.S.C. § 112, first paragraph as allegedly not enabled. Specifically, the Examiner argued that synthesizing an oligonucleotide with a donor and acceptor on the same nucleotide was not enabled.

While Applicants strongly disagree with the Examiner's assessment of the art, to expedite prosecution, claims 16 and 18 are canceled. Claims 1 and 3, and claims dependent thereon do not specifically recite that the donor and quencher are on the same nucleotide. Applicants note that the Examiner acknowledged that claims 15 and 17 were enabled. Accordingly, Applicants respectfully request withdrawal of the rejection.

Applicants have also added claims 32-39, which specifically recite that the quencher moiety comprises nitroindole. Claims 33 and 36 specifically recite that the same nucleotide carries both the donor and the nitroindole quencher moiety. Synthesis of an oligonucleotide carrying nitroindole and a donor on the same nucleotide involves only routine techniques as described in Example 2 of the patent application. Example 2 describes addition of nitroindole and the donor fluorscein on the same nucleotide of an oligonucleotide. The technique for achieving this involves first linking the nitroindole moiety to the nucleotide and then adding the donor moiety to the nitroindole moiety using standard phosphoramidate chemistry. Since production of the recited molecules involves only standard chemical syntheses, the enablement requirement for claims 32-39 is fulfilled.

VIII. Rejection under 35 USC § 112, second paragraph

Claims 15-18 were rejected under 35 U.S.C. § 112, second paragraph as allegedly vague.

Claim 15 was rejected as vague because it was allegedly unclear whether "FRET donor entity" and "donor fluorescent entity" were identical. Claim 15 is canceled and the new claims do not recite "donor fluorescent entity". Therefore, withdrawal of the rejection is requested.

Claim 17 was rejected a vague because it is allegedly unclear what oligonucleotide carries the donor entity. Claim 17 is canceled, rendering the rejection moot. However, new claims contain the rejected language.

Applicants submit that the language is clear. The claim allows for either the first or third oligonucleotide to carry the donor. Whichever oligonucleotide carries the donor also carries the "second entity". In some cases the first oligonucleotide carries the donor in which

case the first oligonucleotide also carries the second entity. In some cases the third oligonucleotide carries the donor, in which case the third oligonucleotide also carries the second entity. As the meaning of this language is clear, Applicants respectfully request withdrawal of the rejection.

IX. Rejection under 35 USC § 102

Claims 15, 17 and 19 were rejected under 35 U.S.C. § 102 as allegedly anticipated by Mathies *et al.* According to the Examiner, the "F2R" and "F6R" oligonucleotides anticipate the present claims because each carry a donor (FAM) and an acceptor (ROX). Applicants respectfully traverse the rejection.

As amended, claims 1 and 3 specifically recite that the oligonucleotide carrying the FRET acceptor entity does not carry a FRET donor. The Examiner states that both the F2R and F6R oligonucleotides carry both a donor and acceptor entity. Therefore, the Examiner has not set forth a *prima facie* anticipation rejection of claims 1-6, each of which include a recitation of an oligonucleotide carrying the acceptor, but lacking a donor.

With regard to claims 32-39, the claims recite use of a nitroindole moiety as a quencher. The Examiner has not indicated that the cited referenced teaches or suggests use of a nitroindole moiety and therefore has not set forth a *prima facie* obviousness rejection of claims 32-39.

In view of the arguments above, Applicants respectfully request withdrawal of the rejection.

Appl. No. 10/621,428
Amdt. dated April 4, 2005
Reply to Office Action of November 2, 2004

PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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